

FIGURE 2

	1				50
hCaspase-12	MADEKPSNGV	LVHMKLLIK	TFLDGIFDDL	MENNVLNTDE	IHLIGKCLKF
KW-Ap	MADEKPSNGV	LVHMKLLIK	TFLDGIFDDL	MENNVLNTDE	IHLIGKCLKF
KW-Bp	MADEKPSNGV	LVHMKLLIK	TFLDGIFDDL	MENNVLNTDE	IHLIGKCLKF
KW-Cp	MADEKPSXGV	LVHMKLLIK	TFLDGIFDDL	MENNVLNTDE	IHLIGKCLKF
KW-Dp	MADEKPSNGV	LVHMKLLIK	TFLDGIFDDL	MENNVLNTDE	IHLIGKCLKF
KW-Ep	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Fp	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Gp	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Hp	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Ip	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Jp	MADEKPSNGV	LVHMKLLIK	TFLDGIFDDL	MENNVLNTDE	IHLIGKCLKF
KW-Kp	MADEKPSNGV	LVHMKLLIK	TFLDGIFDDL	MENNVLNTDE	IHLIGKCLKF
	51				100
hCaspase-12	VVSNAENLVD	DITETAQIAG	KIFREHLWNS	KKQLSSALLE	IQGAQPSGKL
KW-Ap	VVSNAENLVD	DITETAQIAG	KIFREHLWNS	KKQLSS....
KW-Bp	VVSNAENLVD	DITETAQIAG	KIFREHLWNS	KKQLSS....
KW-Cp	VVSNAENLVD	DITETAQIAG	KIFREHLWNS	KKQLSS....
KW-Dp	VVSNAENLVD	DITETAQIAG	KIFREHLWNS	KKQLSS....
KW-Ep	~~~~~	~~~~~	~~~~~	~~~~~	----PSGKL
KW-Fp	~~~~~	~~~~~	~~~~~	~~~~~	---AQPSGKL
KW-Gp	~~~~~	~~~~~	~~~~~	~~~~~	---AQPSGKL
KW-Hp	~~~~~	~~~~~	~~~~~	~~~~~	---AQPSGKL
KW-Ip	~~~~~	~~~~~	~~~~~	~~~~~	---AQPSGKL
KW-Jp	VVSNAENLVD	DITETAQIAG	KIFREHLWNS	KKQLSS....
KW-Kp	VVSNAENLVD	DITETAQIAG	KIFREHLWNS	KKQLSSALLE	IQGAQPSGKL
	101				150
hCaspase-12	KLCPHAHFHE	LKTKRADEIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-ApIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-BpIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-CpIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-DpIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-Ep	KLCPHAHFHE	LKTKRADEIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-Fp	KLCPHAHFHE	LKTKRADEIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-Gp	KLCPHAHFHE	LKTKRADEIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-Hp	KLCPHAHFHE	LKTKRADEIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-Ip	KLCPHAHFHE	LKTKRADEIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-JpIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
KW-Kp	KLCPHAHFHE	LKTKRADEIY	PVMEKERRTC	LALNIRNKEF	NYLHNRNGSE
	151				200
hCaspase-12	LDLLGMRDLL	ENLGYSVVIK	ENLTAQEMET	ALRQFAAHPE	HQSSDSTFLV
KW-Ap	LDLLGM*DLL	ENLGYSVVIK	ENLTAQEMET	ALRQFAAHPE	HQSSDSTFLV
KW-Bp	LDLLGM*DLL	ENLGYSVVIK	ENLTAQEMET	ALRQFAAHPE	HQSSDSTFLV
KW-Cp	LDLLGM*DLL	ENLGYSVVIK	ENLTAQ....
KW-Dp	LDLLGM*DLL	ENLGYSVVIK	ENLTAQ....
KW-Ep	LDLLGM*DLL	ENLGYSVVIK	ENLTA....
KW-Fp	LDLLGM*DLL	ENLGYSVVIK	ESLTAQEMET	ALRQFAAHPE	HQSSDSTFLV
KW-Gp	LDLLGM*DLL	ENLGYSVVIK	ENLTAQ....
KW-Hp	LDLLGM*DLL	ENLGYSVVIK	ENLTAQ....
KW-Ip	LDLLGM*DLL	ENLGYSVVIK	ENLTAQEMET	ALRQFAAHPE	HQSSDSTFLA
KW-Jp	LDLLGM*DLL	ENLGYSVVIK	ENLTAQEME.STFLV
KW-Kp	LDLLGM*DLL	ENLGYSVVIK	ENLTAQEMET	ALRQFAAHPE	HQSSDSTFLV

	201				250
hCaspase-12	FMSHGILNGI	CGTKHWDQEP	DVLHDDTIFE	IFNNRNCQSL	KDKPKVIIMQ
KW-Ap	FMSHSILNGI	CGTKHWDQEP	DVLHDDTIFE	IFNNRNCQSL	KDKPKVIIMQ
KW-Bp	FMSHSILNGI	CGTKHWDQEP	DVLHDDTIFE	IFNNRNCQSL	KDKPKVIIMQ
KW-Cp
KW-Dp
KW-Ep	...SILNGI	CGTKHWDQEP	DVLHDDTIFE	IFNNRNCQSL	KDKPKVIIMQ
KW-Fp	FMSHSILNGI	CGTKHWDQEP	DVLHDDTIFE	IFNNRNCQSL	KDKPKVIIMQ
KW-Gp
KW-Hp
KW-Ip	FMSHSILNRI	CGTKHWDQEP	DVLHDDTIFE	IFNNRNCQSL	KDKPK.....
KW-Jp	FMSHSILNGI	CGTKH~~~~	~~~~~	~~~~~	~~~~~
KW-Kp	FMSHSILNGI	CGTKHWDQEP	DVLHDDTIFE	IFNNRNCQSL	KDKPKVIIMQ
	251				300
hCaspase-12	ACRNGAGIV	WFTTDSGKAS	ADTHGRLLQG	NICNDAVTKA	HVEKDFIAFK
KW-Ap	ACRNGAGIV	WFTTDSGKAS	ADTHGRLLQG	NICNDAVTKA	HVEKDFIAFK
KW-Bp	ACRNGAGIV	WFTTDSGKAS	ADTHGRLLQG	NICNDAVTKA	HVEKDFIAFK
KW-CpGAGIV	WFTTDSGKAS	ADTHGRLLQG	NICNDAVTKA	HVEKDFIAFK
KW-DpGAGIV	WFTTDSGKAS	ADTHGRLLQG	NICNDAVTKA	HVEKDFIAFK
KW-Ep	ACRG~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Fp	AC~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-GpGAGIV	WFTTDSGKAS	ADTHGRLLQG	NICNDAVTKA	HVEKDFIAFK
KW-HpGAGIV	WFTTDSGKAS	ADTHGRLLQG	NICNDAVTKA	HVEKDFIAFK
KW-IpGAGIV	WFTTDVEKAS	ADTHGRLLQG	NICNDAVTKV	HVEKDFIAFK
KW-Jp	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Kp	ACRNGAGIV	WFTTDSGKAS	ADTHGRLLQG	NICNDAVTKA	HVEKDFIAFK
	301				350
hCaspase-12	SSTPHNVSWR	HETNGSVFIS	QIIYYFREYS	WSHHLEEIFQ	KVQHSFETPN
KW-Ap	SSTPHNVSWR	HETNGSVFIS	QIIYYFREYS	WSHHLEEIFQ	KVQHSFETPN
KW-Bp	SSTP.....VQHSFETPN
KW-Cp	SSTPHNVSWR	HETNGSVFIS	QIIYYFREYS	WSHHLEEIFQ	KVQHSFETPN
KW-Dp	SSTP.....VQHSFETPN
KW-Ep	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Fp	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Gp	SSTP.....VQHSFETPN
KW-Hp	SSTPHNVSWR	HETNGSVFIS	QIIYYFREYS	WSHHLEEIFQ	KVQHSFETPN
KW-Ip	SSTP.....VQHSFETPN
KW-Jp	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
KW-Kp	SSTPHNVSWR	HETNGSVFIS	QIIYYFREYS	WSHHLEEIFQ	KVQHSFETPN
	351		374		
hCaspase-12	ILTQLPTIER	LSMTRYFYLF	PGN*		
KW-Ap	ILTQLPTIER	LSMTRYFYLF	PGN*		
KW-Bp	ILTQLPTIER	LSMTRYFYLF	PGN*		
KW-Cp	ILTQLPTIER	LSMTRYFYLF	PGN*		
KW-Dp	ILTQLPTIER	LSMTRYFYLF	PGN*		
KW-Ep	~~~~~	~~~~~	~~~~~		
KW-Fp	~~~~~	~~~~~	~~~~~		
KW-Gp	ILTQLPTIER	LSMTRYFYLF	PGN*		
KW-Hp	ILTQLPTIER	LSMTRYFYLF	PGN*		
KW-Ip	ILTQLPTIER	LSMTRYFYLF	PGN*		
KW-Jp	~~~~~	~~~~~	~~~~~		
KW-Kp	ILTQLPTIER	LSMTRYFYLF	PGN*		

L_a_aln

Human Caspase-12 compared to Mouse Caspase-12 with CARD domain, ICE-p20 domain, ICE-p10 domain and Active-site amino acids described.

hCaspase-12	<u>MADEKPSNGVLVHMKLLIKTFLDGIFFDLMENNVLNTDEIHLIGKCLKFVVSNAENLVD</u>	60
mCaspase-12	<u>MAARRTHERDPIYKIKGLAKDMLDGVFDDLVEKNVLNGDELLKIGESASFILNKAENLVE</u>	60
	** . . . : : : * * * : * * * : * * * : * * * : * * * : * * * : * * * : * * * :	
hCaspase-12	<u>DITETAQIAGKIFREHLWNSKKOLS</u> -----	85
mCaspase-12	<u>NFLEKTDMAKGI FAGHIANSOEQLSLOFSNDEDDGPQKICTPSSPSES KRKVEDDEMEVN</u>	120
	:: * . . . : * * * : * * * : * * * : * * * : * * * : * * * : * * * : * * * :	
	↑auto catalytic	
hCaspase-12	----- <u>SALLEIQGAQPSGKLKLC PHAHFHELKTKRADEIYPVMEKERRTCLALN</u>	134
mCaspase-12	<u>AGLAHESHLMLTAPHGLQSSEVQDTLKLCPRDQFCKIKTERAKEIYPVMEKEGRTLALI</u>	180
	: * : * . . . : * * * : * * * : * * * : * * * : * * * : * * * : * * * :	
	↑calpain	
hCaspase-12	<u>IRNKEFNYLHNRNGSELDLLGMRDLENLGYSVVIKENLTAQEMETALROFAAHPEHOSS</u>	194
mCaspase-12	<u>ICNKKFDYLFDRDNADTDILNMQELLENLGYSVVLKENLTAQEMETELMQFAGRPEHOSS</u>	240
	* * * : * * * : * * * : * * * : * * * : * * * : * * * : * * * : * * * : * * * :	
hCaspase-12	<u>DSTFLVFMSHGILNGICGTXHWDQEPDVLHDDTIFEIFNNRNCOSLKD KPKVIIMQACRG</u>	254
mCaspase-12	<u>DSTFLVFMSHGILEGICGVKHRNKKPDVLHDDTIFKIFNNSNCRSLRNKPKILIMQACRG</u>	300
	***** : * * * : * * * : * * * : * * * : * * * : * * * : * * * : * * * :	
hCaspase-12	<u>NGAGIVWFTTDSGKASADTHGRLLQGNICNDAVTKAHVEKDFIAFKSSTPHNVSWRHETN</u>	314
mCaspase-12	<u>RYNGTIWVSTNKG IATADTDEERVL SCKWNN SITKAHVETDFIAFKSSTPHNISWKVGKT</u>	360
	. * : * . . . : * * * : * * * : * * * : * * * : * * * : * * * : * * * :	
	↑auto catalytic	
hCaspase-12	<u>GSVFISQIIYYFREYSWSHLEEIFOKVOHSFETPNILTOLPTIERLSMTRYFYLFPGN</u>	373
mCaspase-12	<u>GSLFISKLIDCFKKYCWCYHLEEIFRKVOHSFEVPGELTOMPTIERVSMTRYFYLFPGN</u>	419
	** : * * * : * * * : * * * : * * * : * * * : * * * : * * * : * * * : * * * :	

Legend for Domains as calculated by PFAM

CARD Domain	<u>xxxxxxx</u>
ICE-p20 Domain	<u>yyyyyyy</u>
ICE-p10 Domain	<u>zzzzzzz</u>

Active-Site Residues: H...C
 Calpain and Auto-catalytic cleavage sites determined for Mouse Caspase-12

FIGURE 3

H12_a~1

CLUSTAL W (1.7) multiple sequence alignment

```

h_Caspase-3 -----
h_Caspase-7 -----
h_Caspase-12 -----MADE
m_Caspase-12 -----MAAR
h_Caspase-4 -----MAEG
h_Caspase-13 -----MAED
h_Caspase-5 -----MFKGILQSGLDNFVINHMLKNNVAGQTSIQTLVPNTDQKSTSVKKD
h_Caspase-1 -----MAD
h_Caspase-6 -----
h_Caspase-8 -----MDFSRNLYDIGEQLDSEDLASLKFLSLDYIPQRKQEPKIDALM
h_Caspase-10 MKSQGQHWYSSSDKNCKVSVREKLLIIDSNLGVQDVENLKFLCIGLVPNKKLEKSSSSASD
h_Caspase-9 -----MDE
h_Caspase-2 -----MAADRGRIRILGVCGM
h_Caspase-14 -----

h_Caspase-3 -----
h_Caspase-7 -----
h_Caspase-12 KPSNGVLVHMVK----LLIKTFLDGI--FDDLMEENVNLNTDEIHLIGKCL-KFVVSNAEN
m_Caspase-12 RTERDPIYKIK---GLAKDMLDGV--FDDLVEKNVLNGDELLKIGESA-SFILNKAEN
h_Caspase-4 N-HRKKPLKVLE---SLGKDFLTGV--LDNLVEQNVNLNWKEEEKKKYYD-AKTEDKVRV
h_Caspase-13 K-HNKNPLKMLE---SLGKELISGL--LDDFVEKNVLKLEEEKKKKIYD-AKLQDKARV
h_Caspase-5 N-HKKKTVKMLE---YLGKDV LHGV--FNYLAKHDVLTLEEEKKKKYYD-AKIEDKALI
h_Caspase-1 KVLKEKRKLFIR---SMGEGTINGL--LDELLQTRVLNKEEMKVKREN-ATVMDKTRA
h_Caspase-6 -----
h_Caspase-8 LFQRLQEKRMLEESNLSFLKELLFRINRLDLLITYLNTRKEEMERELQTPGRAQISAYRV
h_Caspase-10 VFEHLLAEDLLSEEDPFFLAELLYIIR-QKKLLQHLNCTKEEVERLLPTR--QRVSLFRN
h_Caspase-9 ADRRLLRRCLRL-----LVEELQVDQLWDALLSSELFPHMIEDIQRAGSGSRRDQARQ
h_Caspase-2 HPHHQTCLKKNR---VVLAKQLLLSELLEHLLLEKDIITLEMRELIQAKV--GSFSQNV
h_Caspase-14 -----

h_Caspase-3 -----MENTEN-----SVDSK-SIKNLEPKIIH----GSE-----
h_Caspase-7 ----MADDQGCIEEQGVEDSANED-----SVDAPDRSSFVPSLFS----KKKKN-----
h_Caspase-12 LVDDITETAQIAGKIFREHLWNS----KKQLSSALL--EIQGAQ----PSG----K---
m_Caspase-12 LVENFLEKTD MAGKIFAGHIANS----QEQLSLQFSNDEDDGPQKICTPSSPSES KRKV
h_Caspase-4 MADSMQEKQRMAGQMLLTFFNID----QISPNKKAHPNMEAGPP----ESGES-----
h_Caspase-13 LVDSIRQKNQEAGQVFVQTFLNID----KNSTSIKAPETVAGPD----ESVGS-----
h_Caspase-5 LVDSLRL-KNRVAHQMFQTQTLNMD----QKITSVKPLLQIEAGPP----ESAES-----
h_Caspase-1 LIDSVIPKGAQACQICITYICEEDS---YLAGTLGLSADQTS GNYLNMQDSQGVLS SFFPA
h_Caspase-6 -----MSSASGLRRGHPAGGE-----EN-----
h_Caspase-8 MLYQISEEVSRSELRSFKFLQEEISKCKLDDDMNLLDIFIEMEKRVILGEGKLDILKRV
h_Caspase-10 LLYELSEGIDSENKDMIFLLKDSL P-KTEMTSLSFLAFLEKQGK---IDEDNLTCLEDL
h_Caspase-9 LIIDLETRGSQALPLFISCLEDTG----QDMLASFLRTNRQA AKLSKPTLENLTPVVL RP
h_Caspase-2 LLNLLPKRGPQAFDAFCEALRETKQGHLEDMLLTTL SGLQHVLPPLSCDYDL SL PFPVCE
h_Caspase-14 -----

```

FIGURE 4

h_Caspase-3	-----SMDS--GISLDN-----
h_Caspase-7	-----VTMRS--IKTTRDRVPTY----
h_Caspase-12	----- LKLCPHAHFHELKTKRADE ----
m_Caspase-12	EDDEMEVNAGLAHES--HLM---LTAPHGLQSSEVQDTLKLCPRDQFCKIKTERAKE---
h_Caspase-4	-----TDALKLCPHEEFLRLCKERAEE----
h_Caspase-13	-----AATLKLCPHEEFLKLCKERAGE----
h_Caspase-5	-----TNILKLCPREEFLRLCKKNHDE----
h_Caspase-1	PQAVQD-----NPAMPTSSGSEGNVKLCSLEEAQRIWKQKSAE----
h_Caspase-6	-----MTETDAFYKREMFDPAE----
h_Caspase-8	CAQINKSLLKIINDY--EEFSKERSSSLEGSPDEFSNGEELCGVMTISDSPREQDSE---
h_Caspase-10	CKTVVPKLLRNIEKYKREKAIQIVTPPVDKEAESYQGEELVSQTDVKTFLALPQESWQ
h_Caspase-9	EIRK-----PEVLRPETPRPVDIGSGGFGDVGALSLRGNAD---
h_Caspase-2	SCPLYKKLR-----LSTDTVEHSLDNKDGVPCLQVKPCTPEFYQTHFQ----
h_Caspase-14	-----

h_Caspase-3	-----SYKMDYPEMGLCIIINNKN
h_Caspase-7	-----QYNMNFELGKCIINNKN
h_Caspase-12	----- IYPVMEKERRTCLALNIRN
m_Caspase-12	-----IYPVMEKEGRTRLALIICN
h_Caspase-4	-----IYPIKERNNRTRLALIICN
h_Caspase-13	-----IYPIKERKDRTRLALIICN
h_Caspase-5	-----IYPIKKREDRRRLALIICN
h_Caspase-1	-----IYPIMDKSSRTRLALIICN
h_Caspase-6	-----KYKMDHRRRGIALIFNHER
h_Caspase-8	-----SQTLDKVYQMKSKPRGYCLIINHN
h_Caspase-10	NKHAGSNGNRATNGAPSLVSRGMQASANTLNSETSTKRAAVYRMNRNHRGLCVIVNNHS
h_Caspase-9	-----LAYILSMEPCGHCLIINNVN
h_Caspase-2	-----LAYRLQSRPRGLALVLSNVH
h_Caspase-14	-----MSNPRSLEEEKYDMSGARLA

h_Caspase-3	FH-----KSTGMTSRSGTDVDAANLRETFRNLYEVRNK-NDLTREEIVELMRDVSKE
h_Caspase-7	FD-----KVTGMGVRNGTDKDAEALFKCFRSLGFDVIVY-NDCSCAKMQDLLKKASEE
h_Caspase-12	K-----EFNYLHNRNGSELDLLGMRDLENLGYSVVIKENLTAQEMETALRQFAAHP
m_Caspase-12	K-----KFDYLFDRDNADTDILNMQELLENLGYSVVLKENLTAQEMETELMQFAGRP
h_Caspase-4	T-----EFDHLPPrNGADFDITGMKELLEGLDYSVDVEENLTARDMESALRAFATR
h_Caspase-13	T-----EFDHMPPrNGAALDILGMKQLLEGLGYTVEVEEKLTAARDMESVLWKFAARE
h_Caspase-5	T-----KFDHLPARNGAHYDIVGMKRLQLGLGYTVVDEKNLTARDMESVLRAFAARP
h_Caspase-1	E-----EFDSIPRRTGAEVDITGMTMLLQNLGYSVDVKKNLTAASDMTTELEAFARHP
h_Caspase-6	FF-----WHLTLPERRRTCADRDNLTTRFSDLGFEVKCFNDLKAEEILLKIHEVSTVS
h_Caspase-8	FAKAREKVPKLHSIRDRNGTHLDAGALTTTFFELHFEIKPH-DDCTVEQIYEILKIYQLM
h_Caspase-10	F-----TSLKDRQGTHKDAEILSHVFQWLGFVHIHNNVTKVEMEMVLQKQKCNP
h_Caspase-9	FCR-----E-SGLRTRTGSNIDCEKLRRRFSSPHFMVEVKGDLTAKKMVLALLELAQOD
h_Caspase-2	FTG-----EKELEFRSGGDVDHSTLVTLFKLLGYDVHVLCDQTAQEMQEKLQNFQQLP
h_Caspase-14	L-----ILCVTKAREGSEEDLDALEHMFQRQLRFESTMKRDPATAEQFQEELEKFOQAI

* * : : : :

h_Caspase-3
h_Caspase-7
h_Caspase-12
m_Caspase-12
h_Caspase-4
h_Caspase-13
h_Caspase-5
h_Caspase-1
h_Caspase-6
h_Caspase-8
h_Caspase-10
h_Caspase-9
h_Caspase-2
h_Caspase-14

↓
D--HSKRSSFVVCVLLSHGEEG-----IIFGTNG-----PVDLKKITNFFRGDRCRSL
D--HTNAACFACILLSHGEEN-----VIYKDG-----VTPIKDLTAHFRGDRCKTL
E--HQSSDSTFLVFMESHGILN-----GICGTHWDQEPDVLHDDTIFEIFNNRNCQSL
E--HQSSDSTFLVFMESHGILE-----GICGVKHRNKKPDVLHDDTIFKIFNNSNCRSL
E--HKSSDSTFLVLMESHGILE-----GICGTVHDEKKPDVLLYDTIFQIFNNRNCCLSL
E--HKSSDSTFLVFMESHGILD-----GICGTMHSEEPDVLPHYDTIFRTFNNRNCLSL
E--HKSSDSTFLVLMESHGILE-----GICGTAHKKKKPDVLLYDTIFQIFNNRNCCLSL
E--HKTSDSTFLVFMESHGIRE-----GICGKKHSEQVPDILQLNAIFNMLNTKNCPSL
--HADADCFVCVFLSHGEGN-----HIYAYDA-----KIEIQTLTGLFKGDKCHSL
D--HSNMDCFICCILSHGDKG-----IIYGTDG-----QEAPIYELTSQFTGLKCPSL
A--HADGDCVFCILTHGRFG-----AVYSSDE-----ALIPIREIMSHFTALQCPRL
--HGALDCCVVVILSHGCQASHLQFPQAVYGTG-----CPVSVEKIVNIFNGTSCPSL
A--HRVTDSCIVALLSHGVEG-----AIYGVVG-----KLLQLQEVFQLFDNANCPSL
DSREDPVSCAFVVLMAHGREG-----FLKGEDG-----EMVKLENLFEALNNKNCQAL

::: **

h_Caspase-3
h_Caspase-7
h_Caspase-12
m_Caspase-12
h_Caspase-4
h_Caspase-13
h_Caspase-5
h_Caspase-1
h_Caspase-6
h_Caspase-8
h_Caspase-10
h_Caspase-9
h_Caspase-2
h_Caspase-14

↓
TGKPKLFI IQACRG--ELDCGIETDSG-----VDDDMAC-----HKIP
LEKPKLFFI IQACRG--ELDDGIQADSG-----PINDTDANPR-----YKIP
KDKPKVIMQACRG--GAGIVWFTTD-----SGKASADTHG-RLLQGNIC--NDAVTKA
RNKPKILIMQACRGR--YNGTIWVSTN-----KGIATADTDEERVLS---CKWNNSITKA
KDKPKVII IQACRGA--NRGELWVRDSP-----ASLEVASSQSSENLE-----EDAVYKT
KDKPKVII IQACRGA--NRGELWVSDSP-----PALADSFQSSENLE-----EDAVYKT
KDKPKVII IQACRGE--KHGELWVRDSP-----ASLAVISSQSSENLE-----ADSVCKI
VGPVKIFII IQACRG--SPGVVWFKDSV-----GVSGNLSLPTTEEFE-----DDAIKKA
VGPVKIFII IQACRG--QHDVPVIPLDV-----VDNQTEKLDTNITEVD-----AASVYTL
AGKPKVFFI IQACQGDNYQKGIPVETDS-----EEQPYLEMDLS-----SPQTRYI
AEKPKLFFI IQACQGEI QPSVSI EADALN--PEQAPTSLQ-----DSI
GGKPKLFFI IQACGGEQKDHGFEVASTSPEDESPGSNPEPDATPFQEGRLTFDQLDAISSL
QNKPKMFFI IQACRGDETDRGVDQDQDGN-----HAGSPGCEESDAGKE-----KLPKMRL
RAKPKVYII IQACRGEQRDPGETVGGDE-----IVMVIKDSP-----QTI

***: : : ** *

h_Caspase-3
h_Caspase-7
h_Caspase-12
m_Caspase-12
h_Caspase-4
h_Caspase-13
h_Caspase-5
h_Caspase-1
h_Caspase-6
h_Caspase-8
h_Caspase-10
h_Caspase-9
h_Caspase-2
h_Caspase-14

VDA-DFLYAYSTAPGYYSWRNSKDGSWFIQSLCAMLKQYA-DKLEFMHILTRVNRKVATE
VEA-DFLFAYSTVPGYYSWRSPGRGSWFVQALCSILEEHG-KDLEIMQILTRVNDRVARH
HVEKDFIAFKSSTPHNVSWRHETNGSVFISQIIYYFREYS-WSHHLEEIFQ----KVQHS
HVETDFIAFKSSTPHNISWKVGKTGSLFISKLIDCFKKYC-WCYHLEEIFR----KVQHS
HVEKDFIAFCSSTPHNVSWRDSTMGSIFITQLITCFQKYS-WCCHLEEVFR----KVQQS
HVEKDFIAFCSSTPHNVSWRDIKKGSLFITRLITCFQKYA-WCCHLEEVFR----KVQQS
HEEKDFIAFCSSTPHNVSWRDRTRGSIFITELITCFQKYS-CCCHLMEIFR----KVQKS
HIEKDFIAFCSSTPDNVSWRHPTMGSVFIGRLIEHMQEYA-CSCDVEEIFR----KVRFS
PAGADFLMCYSVAEGYYSHRETVNGSWYIQDLCEMLGKYG-SSLEFTELLTLVNRKVSQR
PDEADFLGLMATVNNCVSYRNPAEGTWYIQSLCQSLRERCPRGDDILTILT---EVNVE
PAEADFLGLLATVPGYVSFRHVEEGSWYIQSLCNHLKKLVPRMLKFLEKTM---EIRGR
PTPSDIFVSYSTFPGFVSWRDPKSGSWYVETLDDIFEQWA-HSEDLQSLLL---RVANA
PTRSDMICGYACLKGTAAAMRNTRKGSWYIEALAQVFSERA-CDMHVADMLVKVN-ALIKD
PTYTDALHVYSTVEGYIAYRHDQKGSFCFIQTLVDVFTKRK---GHILELLT---EVTRR

* : : : * : : : : :

H12_b_~1

CLUSTAL W (1.7) multiple sequence alignment

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h_Caspase-4 -----MAEGN-HRKKPLKVLES
h_Caspase-5 MFKGILQSGLDNFVINHMLKNNVAGQTSIQTLVPNTDQKSTSVKKN-HKKKTVMKLEYL
h_Caspase-13 -----MAEDK-HNKNPLKMLES
h_Caspase-12 -----MADEKPSNGVLVHMKLL
h_Caspase-1 -----MADKVLKEKRKLFIRSM
: : : : :

h_Caspase-4 GKDFLTGVLDNLVEQNVLNWKEEEKKKYYDAKTEDKVRVMADSMQEKQRMAGQMLLQTF
h_Caspase-5 GKDVHGVFNVLAKHDVLTLEEEKKKKYYDAKIEDKALILVDSL-KNRVAHQMTQTLL
h_Caspase-13 GKELISGLLDDFVEKNVLKLEEEKKKKYYDAKLQDKARVLVDSIROKNQEAGQVFVQTF
h_Caspase-12 IKTFLDGIFDDLMENNVLNTDEIHLIGKCLKFVVSNAENLVDDITETAQIAGKIFREHLW
h_Caspase-1 GEGTINGLLDELLQTRVLNKEEMKVKRENATVMDKTRALIDSVIPKGAQACQICITYIC
: : *::: : : **..* . . . : *: : . * : : :

h_Caspase-4 N-----IDQISPNKKAHPNMEAG--PPESGESTDALKLCP
h_Caspase-5 N-----MDQKITSVKPLLQIEAG--PPESAESTNLIKLC
h_Caspase-13 N-----IDKNSTSIKAPETVAG--PDESVGSAATLKLCP
h_Caspase-12 N-----SKKQLSS--ALLEIQGA--QP-SGK----LKLCP
h_Caspase-1 EEDSYLAGTLGLSADQTSQNYLNMQDSQGVLSFPAPQAVQDNPAMPTSSSGSEGNVKLCS
: : . . . . * :***.

h_Caspase-4 HEEFLRLCKERAEIYPIKERNNRTRLALII CNTEFDHLP PRNGADFDITGMKELLEGLD
h_Caspase-5 REEFLRLCKKNHDEIYPIKKREDRRRLALII CNTKFDHLP ARNGAHYDIVGMKRLLQGLG
h_Caspase-13 HEEFLKLCKERAGEIYPIKERKDRTRLALII CNTEFDHMP PRNGAALDILGMKQLLEGLG
h_Caspase-12 HAHFHELKTKRADEIYPVMEKERRTCLALNIRNKEFNYLHNRNGSELDLGMRDLENLG
h_Caspase-1 LEEAQRIWKQKSAEIYPIMDKSSRTRLALIICNEEFDSIPRRTGAEVDITGMTMLLQNLG
. :. :. :****: :. * *** * * :*: : *: : * * ** :*.

h_Caspase-4 YSVDVEENLTARDMESALRAFATRPEHKSSDSTFLVLM SHGILEGICGTVHDEKKPDVLL
h_Caspase-5 YTVVDEKNLTARDMESVLRAFAARPEHKSSDSTFLVLM SHGILEGICGTAHKKKKPDVLL
h_Caspase-13 YTVEVEEKL TARDMESVLWKFAAREEHKSSDSTFLVFM SHGILDGICGTMHSEEPDVLP
h_Caspase-12 YSVVIKENLTAQEMETALROFAAHPEHQSSDSTFLVFM SHGILNGICGTKHWDQEPDVLH
h_Caspase-1 YSVDVKKNLTASDMTTELEAFAHRPEHKTSDSSTFLVFM SHGIREGICGKKHSEQVPDILQ
*: * :*:*** :* : * ** : **::*****:***** :****. * : :*: *

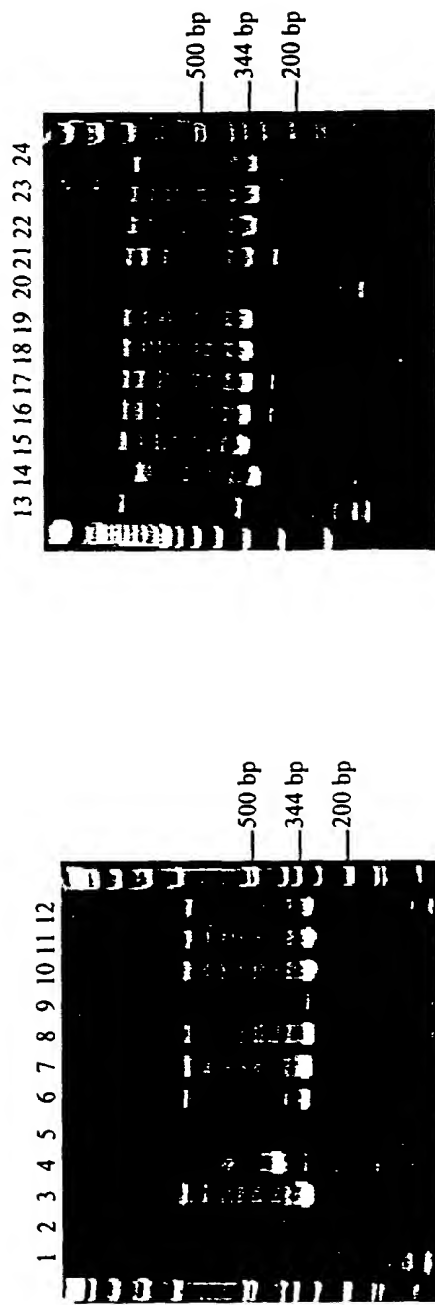
h_Caspase-4 YDTIFQIFNNRNCLSLKDKPKVII VQACRGANRGE LWVR-DSPASLEVASSQSSE-NLEE
h_Caspase-5 YDTIFQIFNNRNCLSLKDKPKVII VQACRGEKHGE LWVR-DSPASLAVISSQSSE-NLEA
h_Caspase-13 YDTIFRTFNRRNCLSLKDKPKVII VQACRGANRGE LWVS-DSPPALADSFSQSSE-NLEE
h_Caspase-12 DDTIFEIFNNRNCQSLKDKPKVIIIQACRGNGAGIVWFTTDSGKASADTHGRLLQGNICN
h_Caspase-1 LNAIFNMLNTKNCPSLKDKPKVIIIQACRGDSPGVVWFK-DSVGVSGNLSLPTTE-EFED
: :*. :*: :* *****:***** * :. ** : : :

h_Caspase-4 DAVYKTHVEKDFIAFCSSTPHNVSWRDSTMGSI FITQLITCFQKYSWCCHLEEVFRKVQ
h_Caspase-5 DSVCKIHEEKDFIAFCSSTPHNVSWRDRTRGSI FITELITCFQKYSWCCCHLMEIFRKVQ
h_Caspase-13 DAVYKTHVEKDFIAFCSSTPHNVSWRDIKKGSLFITRLITCFQKYAWCCHLEEVFRKVQ
h_Caspase-12 DAVTKAHVEKDFIAFKSSTPHNVSWRHETNGSVFISQIIYYFREYSWSHHLEEFQKVQH
h_Caspase-1 DAIKKAHIEKDFIAFCSSTPDNVSWRHPTMGSVFIGRLIEHMQEYACSCDVEEIFRKVRF
*: : * * ***** ***** . **:* :* :*: :. :*: :*:

h_Caspase-4 SFETPRAKAQMPTIERLSMTRYFYLFPGN
h_Caspase-5 SFEVPOAKAQMPTIERATLTRDFYLFPGN
h_Caspase-13 SFEKPNVKAQMPTVERLSMTRYFYLFPGN
h_Caspase-12 SFETPNILTQLPTIERLSMTRYFYLFPGN
h_Caspase-1 SFEQPDGRAQMPTTERTVTLTRCFYLFPGH
*** * :*:** ** :*:*****:

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Tissue Profiling of hCaspase-12



1. Brain 2. Heart 3. Kidney 4. Spleen 5. Liver 6. Colon 7. Lung 8. Small Intestine
9. Muscle 10. Stomach 11. Testis 12. Placenta 13. Pituitary 14. Thyroid gland
15. Adrenal gland 16. Pancreas 17. Ovary 18. Uterus 19. Prostate 20. PBL 21. Fetal brain 22. Fetal liver 23. Fat 24. Mammary gland

FIGURE 6

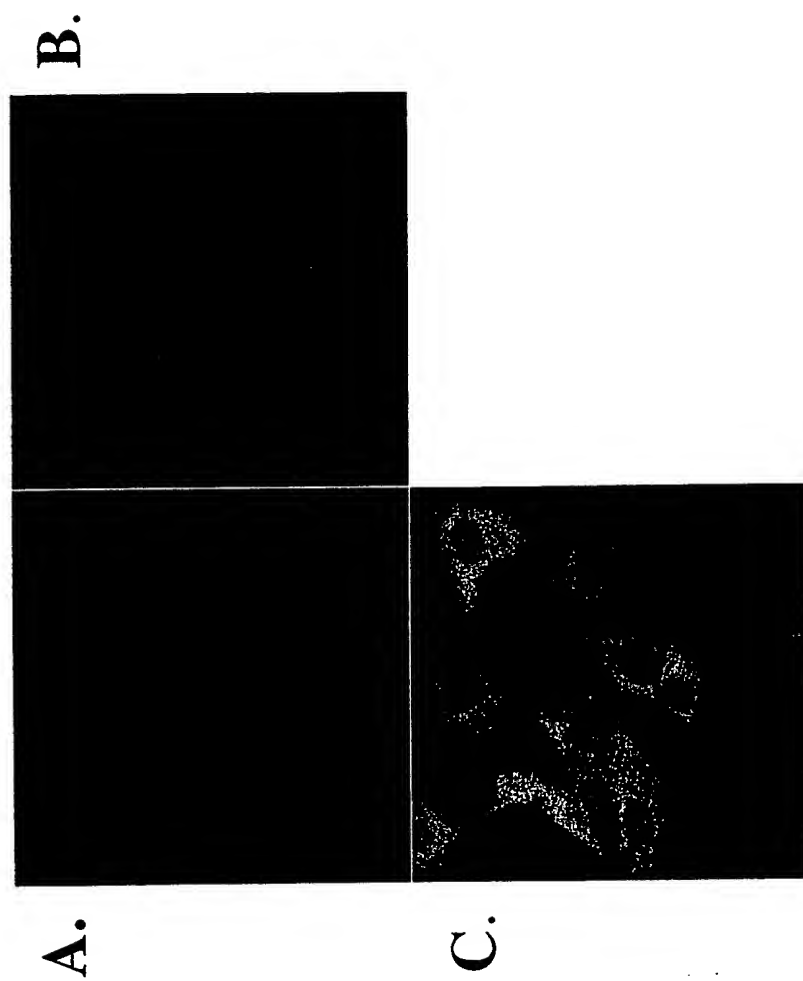


FIGURE 7

SH-EP cell transfection +/- α -Fas

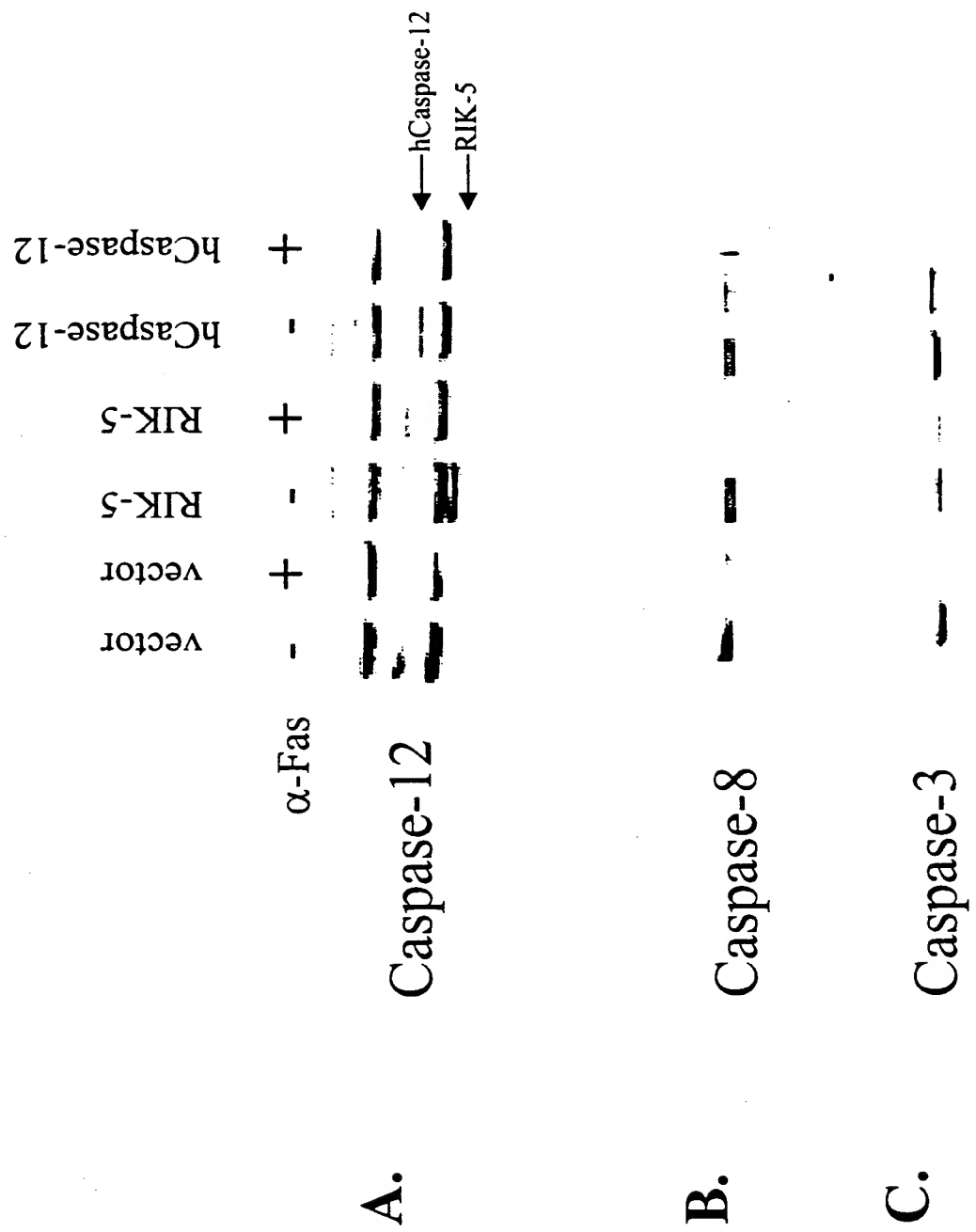


FIGURE 9

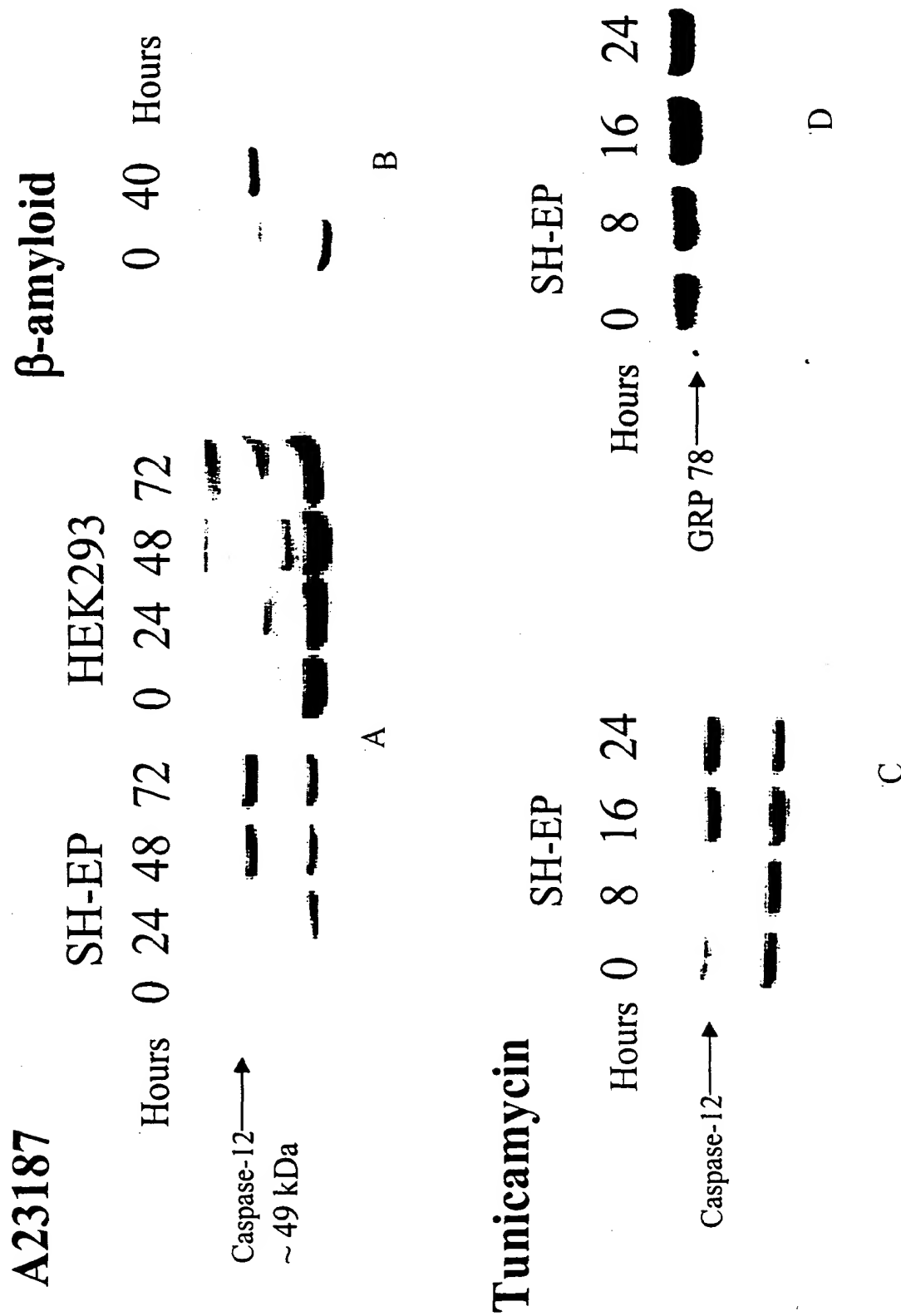


FIGURE 10

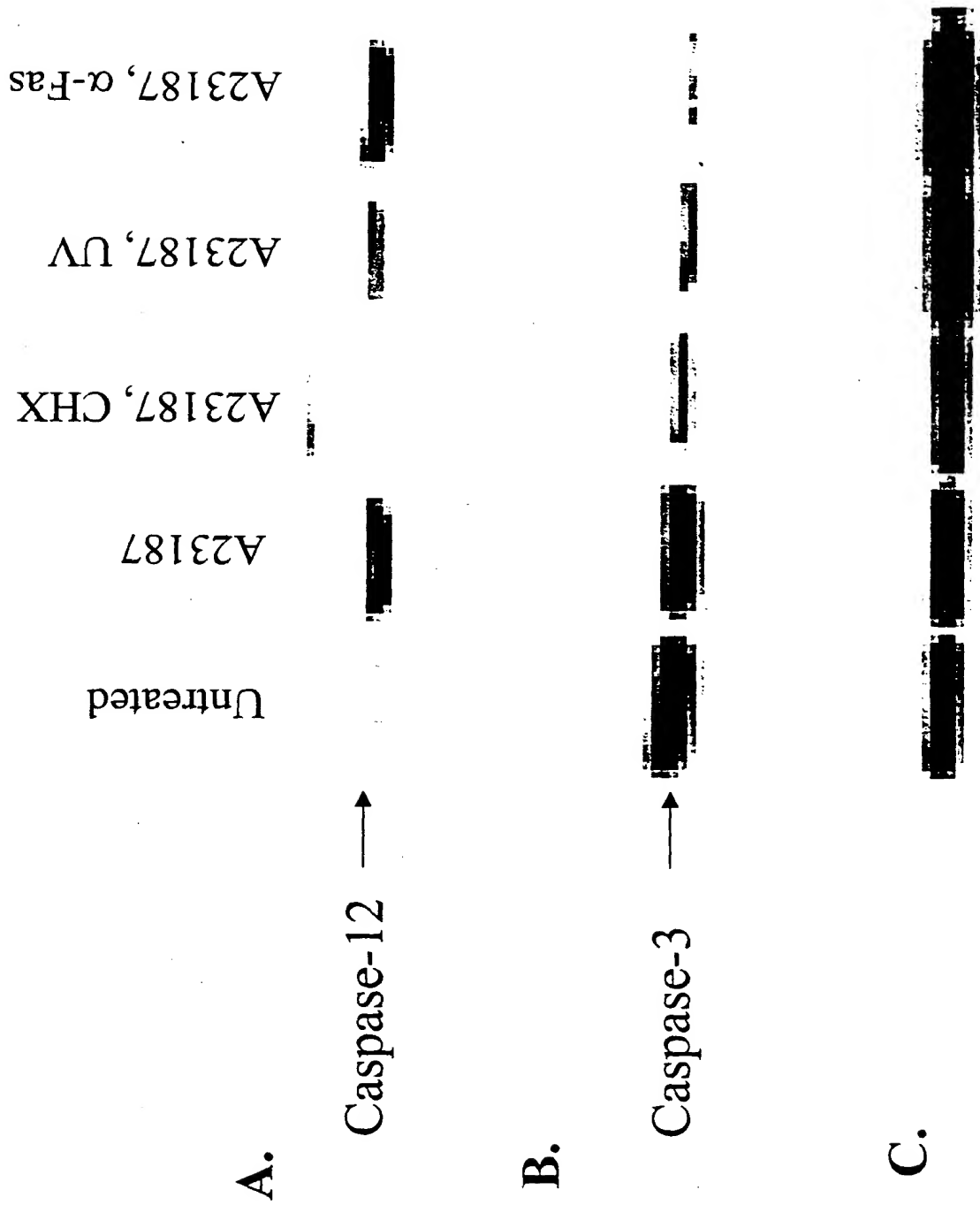


FIGURE 11

SH-EP cells treated with A23187, UV +/- inhibitors

A.

1. 2. 3. 4.

Caspase-12



B.

Caspase-3



Calpain cleavage of recombinant caspase-12

